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MORAN, MARJORIE A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/267,199	Applicant(s) BHAT ET AL.	
	Examiner Marjorie Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,10-18 and 20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10-18 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All rejections and objections not repeated below are hereby withdrawn. Claims 1-2, 10-18, and 20-26 are pending. Applicant is thanked for clarifying the status of claims 3-9 and is requested to place all amendments to the claims, including requests for cancellation, on a page or pages separate from argument or remarks pages in future communications.

Claim Rejections - 35 USC § 112, 2nd paragraph

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 recites an isolated nucleic acid molecule "consisting essentially of" residues from a selected group. The phrase "consisting essentially of" is generally used to refer to a composition comprising different elements or compounds or to a method comprising different method steps. The phrase is not defined by the specification, and it is unclear what elements of a nucleic acid sequence are intended to be included or excluded by use of the phrase, therefore use of the phrase renders the claim indefinite. For purpose of further examination, claim 26 will be interpreted as if it recited a "nucleic acid molecule comprising residues..." See MPEP 2111.03, which states:

"The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In re Herz, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original)... "A consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and

fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco, Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) "

35 U.S.C. 101/112 Utility Rejections

Claims 2, 10-18 and 20-22 are again rejected, as previously set forth in the office action of 6/5/01, and new claims 24-26 are newly rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or by a well established utility.

Applicant's arguments filed 1/17/02 have been fully considered but they are not persuasive.

In response to applicant's arguments that the specification clearly asserts that the claimed nucleic acids encode tocopherol synthesis pathway enzymes, it is admitted that this is a utility asserted by the specification. The asserted utility, however, is not a substantial, specific, and credible utility for the reasons previously set forth. Any nucleic acid molecule encoding an ATG codon could theoretically encode a peptide. However, it is well known in the art that a nucleic acid molecule actually encodes a peptide only if an ORF is present; i.e. the "ATG" is read in the correct "frame" and there is a "stop" codon such that translation of the peptide starts and stops correctly. For the nucleic acid to have utility based on the peptide thus encoded, the peptide must have utility. That is, the identity and activity of the peptide must be known or established. A fragment of a protein, wherein the fragment itself does not have utility or activity, does not necessarily have a utility.

In the instant case, it is asserted that the claimed nucleic acid molecules encode tocopherol synthesis pathway enzymes or fragments thereof. Each nucleic acid molecule claimed has at least one (inmost cases, several) ATG "codons". However, it is not known for ANY of the claimed sequences what the ORF is, therefore it is unknown whether any sequence is actually translated into a peptide, or, if translated, what the activity or function of that peptide may be. For example, SEQ ID NO: 161 comprises six "ATG' codons, but it is not known which, if any, is the start codon for a tocopherol synthesis pathway enzyme. Page 241 of the specification discloses that a putative peptide encoded by SEQ ID NO: 161 is 69% identical to a shikimate kinase enzyme from yeast, but there is no disclosure or evidence anywhere that that peptide so encoded has kinase activity, specifically shikimate kinase activity, or would be expected to have kinase activity (e.g. based on comparison of tertiary structures, active regions, conserved domains, etc.) It is possible that SEQ ID NO: 161 encodes a fragment of a shikimate kinase; however, it is not disclosed whether that fragment has activity or another function that the fragment has utility under 35 USC 101.

As previously set forth, homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence. See p. 7 of the office action of 11/21/00 regarding lack of predictability based on sequence homology. The prior art does not teach that the elected SEQ ID's encode the alleged proteins and the specification does not show that the

peptides putatively encoded by the claimed nucleic acid sequences have an activity or function similar to those to which they are homologous.

Arguments with regard to genotyping and in re Brana (34 USPQ2d 1436) were addressed in the previous office action. With regard to in re Gaubert (187 USPQ 664), it is noted that the fact patterns are not the same as those of the instant case. The Gaubert case was concerned with a machine wherein the operability of a specific part was in question. As there were alternate ways of arriving at operability of the piece of machinery in question, the machine as a whole was deemed to have utility. The utility of the machine was not predicated on utility of the product made. In the instant case, the question of utility is not based on inoperability of a portion of a nucleic acid, but rests on whether the claimed nucleic acids, themselves, have utility, or encode proteins which have utility.

As the instant specification does not disclose, and the prior art does not teach, that the instantly claimed nucleic acid sequences actually encode any protein or peptide, specifically the enzymes recited in Table A, the nucleic acid sequences represented by SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232 do not have utility based on utility of a protein encoded thereby.

For all of the reasons previously set forth and set forth above, the rejections of claims 2,10-18, and 20-22 is maintained and new claims 24-26 are rejected.

Claims 2,10-18, 20-22, and 24-26 are also rejected under 35 U.S.C. 112, first paragraph for not being enabled.

Applicant's arguments filed 1/17/02 have been fully considered but they are not persuasive. This enablement rejection is linked to the utility rejection, as previously set forth. As the utility rejection is maintained, the enablement rejection is also maintained.

Claim Rejections - 35 USC § 112, 1rst paragraph

New claim 26 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A nucleic acid molecule "consisting essentially of" residues from a selected group of sequences is new matter. The originally filed claims do not recite any nucleic acid molecules or sequences "consisting essentially of" specific residues, the specification does not define what is meant by a nucleic acid molecule "consisting essentially of" certain residues (see 112, 2nd rejection), applicant fails to point to specific support for this limitation in the instant specification, and no support is apparent. As no support is provided by the originally filed claims or specification for a nucleic acid molecule "consisting essentially of" particular residues, claim 26 recites new matter.

Claims 1-2 are again rejected, and new claims 23-24 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

Applicant's arguments filed 1/17/02 have been fully considered but they are not persuasive. Applicant argues that he was in possession of the claimed nucleic acid sequences and points to Table A as (apparent) evidence that these sequences encode the claimed enzymes. In response, it is noted, as previously set forth and reiterated above, that the instant specification does not teach that any of SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 184, 199, and 232 actually encode any protein or peptide, specifically the enzymes recited in claims 1 and 23. Again, it is noted that homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence. With regard to Table A, the highest percent homology shown between any peptide putatively encoded by one of the claimed sequences and a known protein is 81% (for the peptide putatively encoded by SEQ ID NO: 232), while the lowest shown is 40% (for the peptide putatively encoded by SEQ ID NO: 147). While 80% certainly represents a peptide which would reasonably be expected to be related to the known protein (e.g. by having one or more structural motifs in common), it is not evidence that an enzyme with chorismate synthase activity is actually encoded by and translated from the SEQ ID NO: 232. One of skill in the art would reasonably doubt whether a peptide which is only 40%

homologous to another is indeed a protein with similar activity. In response to applicant's argument that those skilled in the art "routinely" characterize function based on sequence homology, it is noted that due to the level of unpredictability in the art, one skilled in the art may *postulate* function based on sequence homology, but cannot "routinely" (consistently) and *accurately predict* function based on homology alone. See IBBA (TIBS (2002), vol. 27 (2), page 64) for support that, as recently as Feb. 2002, there was controversy in the art over prediction of function based on sequence homology.

Applicant argues that a detailed chemical structure; i.e. the claimed nucleic acid sequences are disclosed in the instant specification. While the nucleic acid sequences represented by the claimed SEQ ID NO's are fully described by the specification at the time of filing, nucleic acid sequences *encoding the proteins* recited in claims 1 and 23 were not fully described as set forth above. The specification does not disclose that the claimed nucleic acid sequences actually encode any proteins or peptides, as previously set forth and reiterated above, therefore nucleic acid sequences encoding the claimed proteins AND comprising the claimed SEQ ID NO's were not described in the specification as originally filed. For the reasons set forth above, the rejection of claims 1-2 is maintained and claims 23-24 are rejected.

Claims 1-2,10-18, 20-24 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The specification discloses SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232. The specific sequences corresponding to SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232 meet the written description provisions of 35 USC 112, first paragraph. However, claims 2 and 10-22 recite open claim language (i.e. comprising, comprises, or having) and are therefore also directed to encompass gene sequences, sequences that hybridize SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232, corresponding sequences from other species, derivatives, allelic variants, splice variants, and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claims.

With regard to claim 1, the specification discloses on pages 2-11 that the various enzymes recited in the claims are known and have been isolated from various sources. Page 7 of the specification discloses that the gene encoding hydroxyphenylpyruvate dioxygenase has been identified, but does not disclose the source of the gene. Page 8 discloses that the gene for geranylgeranyl-pyrophosphate synthase has been isolated from Arabidopsis and C. roseus. The specification does not disclose nucleic acid sequences encoding any of the maize or soybean enzymes recited in claim 1, as set forth above. The prior art teaches several nucleic acid sequences encoding maize or soybean enzymes, as set forth below; however, these sequences are not recited in the instant specification nor are the references teaching them incorporated by reference. Neither the prior art nor the instant specification teach nucleic acid sequences encoding the proteins designated in amended claim 1 as (b)-(m), therefore nucleic acids encoding these proteins are not described at all. No amino acid sequences are taught in the instant specification. Claim 1 is directed to encompass many variants, mutations, deleted sequences, etc. as long as those sequences encode one of the recited proteins. As it is unknown how many or what variants may exist for each of the recited proteins, one skilled in the art would not be able to envision all of the embodiments represented by claim 1. The specification fails to provide sufficient written description to support the limitations of the claim.

Applicant's arguments filed 1/17/02 have been fully considered but they are not persuasive. In response to applicant's arguments that the specification provides a detailed chemical structure; i.e. sequence, of each of the claimed nucleic acids, the examiner maintains that the rejected claims encompass sequences/structures such as corresponding sequences from other species, derivatives, allelic variants, splice variants, and so forth, which are not fully and completely described by the instant specification, as set forth above, therefore the rejection of claims 1-2, 10-18 and 20-22 is maintained and claims 23-24 and 26 are rejected.

Claim 2 is again rejected and new claim 24 is newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an ENABLEMENT rejection.

Applicant's arguments filed 1/17/02 have been fully considered but they are not persuasive. In response to applicant's argument Table A discloses that the claimed nucleic acid sequences encode the proteins claimed, it is again noted that homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence, and that the instant specification does not disclose anywhere that the claimed nucleic acids actually encode any peptide or protein, as previously set forth and reiterated above. Also as previously set forth, while the prior art teaches isolated nucleic acid sequences which encode the corn or soybean enzymes recited in the claims, the sequences taught by the prior art are not the same as those recited in the instant claims. In response to the argument that "there are only three possible reading frames for each nucleic acid strand", it is noted that each nucleic acid claimed comprises several ATG codons, any of which may be a possible start site for translation into a peptide. It is known in the art that nucleic acids (genes) from eukaryotic organisms often comprise multiple open reading frames, (i.e. multiple start and/or stop codons), therefore one skilled in the art to must determine, for any given sequence, which open reading frame to use to generate a peptide. Given an amino acid sequence for a particular peptide, it would require fairly routine experimentation to "line up" the encoding polynucleotide with the peptide sequence to determine which portion of the nucleic acid sequence comprises the coding region for the peptide. The instant specification does not disclose any amino acids sequences. As no information which would allow one skilled in the art to determine how to generate the specific peptides used for the homology comparisons of Table A of the instant specification, it would require undue experimentation for one skilled in the art to determine how to generate the peptides, with the functionality claimed, from the disclosed nucleic acid sequences.

In response to the arguments that activity assays for the claimed enzymes are well known in the art, and therefore need not be taught by the instant specification, it is again noted that while assays to determine kinase activity are known in the art, each is specific to a particular substrate. An assay to detect tyrosine kinase activity would not necessarily detect shikimate kinase activity, therefore one skilled in the art would have to develop an assay to determine if a kinase with the claimed functionality and specificity (e.g. a shikimate kinase as opposed to a tyrosine kinase) were indeed produced. As previously set forth, the level of skill in the art is acknowledged to be high. Sequences encoding some of the maize or soybean proteins set forth in claim 1 are known in the art; however, these are not the sequences recited in the claims. One skilled in the art would therefore (a) have to determine which portion of a

particular SEQ ID NO: encodes a specific protein, (b) determine if the protein produced is the same as that recited in Table A (e.g. determine if the homology "matches" that disclosed), (c) determine whether the protein produced is an enzyme with the functionality and specificity recited in the claims. As the one skilled in the art must "guess" at some information (e.g. open reading frames, actual start codon, homology parameters) and/or develop new assays to arrive at the claimed invention, it would require undue experimentation for one skilled in the art to know how to make and use the claimed invention. For these reasons and those previously set forth, the rejection of claim 2 is maintained and claim 24 is rejected.

Claim Rejections - 35 USC § 102

Applicant has not set forth any arguments or amendments to overcome the rejections below, therefore the rejections are maintained.

Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by BAYSDORFER (Genbank accession no. AA661448, 11/12/1997).

BAYSDORFER teaches an mRNA sequence from maize encoding 3-deoxy-d-arabino-heptulosonate 7-phosphate synthase, thereby anticipating claim 1. BAYSDORFER's sequence is an mRNA with complementarity to instant SEQ ID NO: 1, and would be expected to hybridize to SEQ ID NO: 1 under the conditions recited in instant claim 10, therefore claim 10 is also anticipated.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by SASAKI (Genbank accession no. D39938, 11/11/1994).

SASAKI teaches a cDNA sequence which is 87.7% identical to instant SEQ ID NO: 1, and would be expected to hybridize under the conditions recited in instant claim 10 to a complement of SEQ ID NO: 1, therefore claim 10 is anticipated.

Conclusion

No claims are allowed.

It is noted that the specification contains an embedded hyperlink and/or other form of browser-executable code (i.e. "active" URL's) on page 16. Applicant is hereby notified that the embedded hyperlink and/or other form of browser-executable codes will need to be deleted or amended to a "non-active" format before any indication of allowability can be made.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a patent analyst, Tina Plunkett, whose telephone number is (703) 305-3524.

Marjorie A. Moran
Examiner
Art Unit 1631

April 8, 2002

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER